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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,303	07/06/2001	Geert Maertens	2752-52	3515

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,303	MAERTENS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-70,73,74,76,77,79,85-91 and 95-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-70,73,74,76,77,79,85-91 and 95-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08612,973 & 08/928,017.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 68-70, 73-74, 76-77, 79, 85-91 and 95-101 are pending

Response to Amendment

This is a response to the amendment, paper No. 25, filed 04/14/04. Claims 68, 69, 70, 73, 76-77 have been amended. Claims 1-67, 71-72, 75, 78, 80-84 and 90-94 have been canceled. Regarding the newly added. Claims 68-70, 73-74, 76-77, 79, 85-91 and 95-101 are considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 102

1. Claims 70, 73, 76, 87, and 95-97 are still rejected under 35 U.S.C. 102(e) as being anticipated by Watanabe et al. (US Patent No. 5,610,009A) on the same ground as stated in the previous Office Action.

2. Applicants traverse the rejection and submit that Watanabe discloses an internal deletion from the HCV E1 protein covering amino acids 260-296 of the HCV polyprotein. Applicants believe the deleted region after plus or minus 8 amino acids should be broadly interpreted as at least including the following nine possibilities: 1). 264-293, 2). 264-285, 3). 264-301, 4). 272-293, 5). 272-285, 6). 272-301, 7). 256-293, 8). 256-285 and 9). 256-301. Applicants asserted therefore, even if construed in its broader sense, none of the claimed possibilities are believed to be identical to the deletion of the cited prior art covering amino acids 260-296 such that the cited art is not believed to teach each and every aspect of the presently claimed invention over Watanabe et al.

3. Applicants' argument has been fully considered; however, it is not persuasive because the HCV E1 protein covering the amino acids 260-296 is just within the range of the last possibility of 256-301. Moreover, the claims as drafted does not read that the vector only allow to express the HCV E1 envelope. The vector that examiner cited in the previous office Action is pHCV419 disclosed in line 47-52 of col. 12. The pHCV416 is a typographic error. pHCV419 is a cloned vector that is constructed by removing an internal hydrophobic region of HCV E1 envelope and

carry the HCV sequence of 192-259, 297-336 and 393-654. In this context, the vector disclosed by Watanabe et al. contains HCV E1 envelope with deletion of its fist hydrophobic domain ranging from amino acid residues 260-296, which meets the limitation of claim 70. The rejection is therefore, maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 68-70, 73-74, 76, 79, 87-88, 91 and 95-96 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Lanford et al. (Virology 1993, Vol. 197, pp. 225-235), Ralston et al. (J. Virol. 1993, Vol. 67, pp.6753-6761), Watanabe et al. (US Patent No. 5,610,009A) and Ford et al. (Protein expression and purification 1991, Vol. 2, pp. 95-107) under the same ground as stated in the previous Office Action.

6. Applicants traverse and submit that the Examiner's combination of 4 references to allege the obviousness of the presently claimed invention fail to provide a prima facie case of obviousness and the Section 103 rejection should be withdrawn. The Examiner's apparent picking and choosing of details from references is believed to be inappropriate and the cited art is not believed to have provided a motivation to one of ordinary skill in the art to have made the presently claimed invention. The Examiner fails to teach how each limitation of rejected claims is anticipated by the cited references. For example, The Examiner does not separately however assert that these claims are anticipated by Lanford. See, paragraph 11 of Paper No. 24. The Examiner further asserts that Ralston "meets the limitation of claims 68 and 88. See, paragraph 12 of Paper No. 24. The Examiner does not separately make a rejection of these claims under Section 102 over Ralston. Similarly, the Examiner asserts that the "Iimitation of claim 74" is

taught by Ford. No. 24. Finally, the Examiner asserts that the "limitation of claim 70" is allegedly taught by Watanabe. See, paragraph 14 of Paper No. 24.

7. Applicants' argument has been considered; however, it is not found persuasive because how each limitations are taught by the cited references are clearly discussed in the first office actions mailed on April 24, 2003.

8. For example, office cited that Lanford et al. teach a recombinant live eukaryotic vector, carrying an HCV E1 protein fragment encoding HCV amino acids 117-386 or 117-340, which is part of SEQ ID NO: 7. in which the 1st hydrophobic domain located at the carboxyl terminal located after amino acid residue of 340 was deleted. The 5' of inserted HCV cDNA fragment contains an ATG for initiation site and the 3' contains a TAA termination codon. The expressing vector is baculovirus vector, which allows the expression of an HCV E1 as a single envelope viral protein (See pages 226-227). These teach the limitations of structural characteristic of claimed HCV envelop that is expressed by a vector of 68, 69, 70, 73, 87, 95, 96, 97.

9. While it does not teach that the vector is a vaccinia viral vector, the vaccinia viral vector used for expressing the HCV envelope protein is well known and commonly used in the art as evidenced by Ralston et al. They teach to use a vaccinia viral vector for expressing HCV E1 protein (See entire document), which meet the limitation of 68 and 88.

10. Regarding the limitation of adding a histidine codon at the C-terminal of claim 74, Office states that the art of adding a tag, such as histidine tag, is also well known and disclosed as a routine technology for producing a recombinant protein for the purpose of convenient purification procedure as evidenced by Ford et al. which is a powerful technique based on interactions of some proteins with immobilized transition metal ions. For example, Ford et al. particularly teach the technique of adding poly(his) tails ranging in length from 2 to 6 residues and fused to either the N-terminus or C-terminus (See section of 7 Poly(His) Tails on page 100), therefore, it greatly benefit for the purification process by using a metal affinity chromatography (IMAC). Therefore, Ford et al. teach the limitation of claim 74.

11. Regarding to the limitation of HCV E1 protein containing a deletion at the amino acid sequence between the positions of 264-293, plus or minus 8 amino acids (272-301 for plus amino acids or 256-285 for minus 8 amino acids), Office further extends the explanation. Watanable al. teach a recombinant live eukaryotic adenovirus vector carrying deferent fragments of HCV E1

protein. Some of them start with the amino acid position 192 originated from the whole genome of HCV cDNA and ends with amino acids 337 or 383 (See lines 16-29 on col. 12), in which a carboxyl terminal of amino acid residue 260-296 to remove the internal hydrophobic region, which is just within the range of the last possibility of amino acid deletion 256-301 as applicants argued in the last response.

12. Because the claims as drafted do not read that the vector only allow to express the HCV E1 envelope. The vector that examiner cited in the previous office Action is pHCV419 disclosed in line 47-52 of col. 12. The pHCV416 is a typographic error. pHCV419 is a cloned vector that is constructed by removing an internal hydrophobic region of HCV E1 envelope and carry the HCV sequence of 192-259, 297-336 and 393-654. In this context, the vector disclosed by Watanabe et al. contains HCV E1 envelope with deletion of its fist hydrophobic domain ranging from amino acid residues 260-296, which meets the limitation of claim 70.

1. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the technique for expressing a recombinant HCV envelope protein and the structural characteristics of the HCV envelope protein are all well disclosed and taught by the prior art, to express different sequences of already known HCV envelope protein due to its well known immunogenic utility are so obvious to any one skill in the art for being motivated to do with expected result. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results. The rejection is maintained.

Claim Rejections - 35 USC § 112

13. Claims 77 and 98-101 are still rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention. In the instant case, the specification does not teach that claimed products are enable to be used as vaccine.

14. Applicants traverse the rejection and submit that the Examiner's apparent requirement for FDA approval in paragraph 20 on page 6 of Paper No. 24 is not believed to be the standard for enablement or written description. Reconsideration and withdrawal of the Section 112, first paragraph rejection are requested.

15. Applicants' argument has been considered; however, it is not persuasive because the specification lacks evidence to support that the claimed immunogenic composition is a vaccine that is able to induce a protective immune response for the HCV infection. Furthermore, the state of art does not teach that the recombinant HCV polypeptide or polyprotein can induce any protective immune response. The rejection is therefore, maintained.

16. In regarding to claim 101, which is inadvertently omitted in the previous Office Action. Because it depends on claim 100, it should also be rejected under 112 1st paragraph because it involves the same issue of enablement of using the claimed composition as a vaccine. Examiner apologizes for the inconvenient by this mistake.

Claim Rejections - 35 USC § 112

17. Claims 95, 96, and 97 are still rejected for being vague and indefinite.

18. Applicants traverse the rejection and submit that specification make clear that parts of the nucleotide sequences recited in claims 95-97 will be understood to encode at least one HCV epitope of the E1 region. The claims are submitted to be definite, especially in light of the specification pages 3-4.

19. The specification of pages 3-4 has been reviewed. There is no definition or explanation about what the "part thereof" means. Therefore, the claims can be explained as any HCV envelope protein as long as it contains a part of listed sequences even if a sequence only contains one amino acid residue of a sequence listed SEQ ID NO in claims 95-97. Therefore, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James C. Housel 6/8/04

Bao Qun Li
Art Unit 1648
June 16, 2004

JAMES HOUSEL
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